

Claims

1. Use of an inhibitor of a receptor tyrosine kinase ligand for the manufacture of a medicament for the prevention or treatment of an at least partially therapy-resistant hyperproliferative disorder.
2. The use of claim 1 wherein the disorder is cancer.
3. The use of claims 1 or 2 wherein the disorder is an at least partially irradiation and/or medicament-resistant cancer.
4. The use of any one of claims 1 to 3 wherein the disorder is at least partially resistant against apoptosis-inducing therapy.
5. The use of any one of claims 1 to 4 wherein the disorder is at least partially resistant against administration of cytostatic and/or cytotoxic medicaments, particularly apoptosis-inducing medicaments.
6. The use of any one of claims 1 to 5 wherein the inhibitor of a receptor tyrosine kinase ligand is co-applied with a further therapeutic procedure and/or medicament.
7. The use of claim 6 wherein the medicament is co-applied with an irradiation therapy.
8. The use of claims 6 or 7 wherein the medicament is co-applied with a further anti-cancer medicament, particularly with a chemotherapeutic agent or with an anti-tumour antibody.

9. The use of claim 8 wherein the further anti-cancer medicament is selected from doxorubicin, a taxane, cis/trans-platin or derivatives thereof, 5-fluorouracil, mitomycin D, paclitaxel, etoposide, cyclophosphamide, docetaxel or other apoptosis-inducing drugs or proteins, in particular antibodies .

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10. Use of an inhibitor of a receptor tyrosine kinase ligand for the manufacture of a medicament for increasing the efficacy of therapies against hyperproliferative disorders.

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11. Use of an inhibitor of a receptor tyrosine kinase for the manufacture of a medicament for increasing the sensitivity of hyperproliferative disorders against irradiation and/or medicament treatment.

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12. Use of an inhibitor of a receptor tyrosine kinase ligand for the manufacture of a medicament for the prevention or treatment of a hyperproliferative disorder which is caused by or associated with stress-induced activation of a receptor tyrosine kinase.

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13. The use of claim 12, wherein the stress is an oxidative and/or osmotic stress.

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14. The use of claims 12 or 13, wherein the stress is a p38-mediated stress.

15. The use of claims 12 to 14, wherein the disorder is cancer.

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16. The use of any one of claims 1 to 15 wherein the receptor tyrosine kinase is selected from EGFR and other members of the EGFR family.

17. The use of any one of claims 1 to 6, wherein the receptor is EGFR.
- 5 18. The method of any one of claims 1 to 17 wherein the receptor tyrosine kinase ligand is a ligand binding to the extracellular domain of said receptor tyrosine kinase.
- 10 19. The use of any one of claim 1 to 18 wherein the receptor tyrosine kinase ligand is selected from HB-EGF, EGF, amphiregulin, betacellulin, epiregulin, TGF- α , neuregulin or heregulin.
- 15 20. The use of claim 19 wherein the receptor tyrosine kinase ligand is HB-EGF.
21. The use of any one of claims 1 to 20 wherein the inhibitor is an inhibitor of a metalloprotease capable of cleaving the receptor tyrosine kinase ligand or an inhibitor of regulatory steps upstream of the metalloprotease.
- 25 22. The use of any one of claims 1 to 12 wherein the inhibitor is a direct inhibitor of the receptor tyrosine kinase ligand.
23. The use of any one of claims 1 to 22 wherein the inhibitor acts on the nucleic acid level.
- 30 24. The use of claim 23 wherein the inhibitor is a specific transcription inhibitor, particularly selected from anti-sense molecules, ribozymes or RNAi molecules.
25. The use of claim 24 wherein the inhibitor is a gene inactivator.

26. The use of any one of claims 1 to 22 wherein the inhibitor acts on the protein level.

5 27. The use of claim 26 wherein the inhibitor is a specific protein inhibitor, particularly selected from antibodies or antibody fragments and/or from proteinaceous or low-molecular weight inhibitors.

10 28. A pharmaceutical composition or kit comprising as active ingredients

15 (a) an inhibitor of a receptor tyrosine kinase ligand which is an inhibitor of a metalloprotease capable of cleaving the receptor tyrosine kinase ligand or an inhibitor of regulatory steps upstream of the metalloprotease, and

(b) a further medicament for the treatment of hyperproliferative disorders.

29. The composition or kit of claim 28 which additionally

20 comprises pharmaceutically acceptable carriers, diluents and/or adjuvants.

30. A method of preventing or treating an at least partially therapy-resistant hyperproliferative disorder comprising administrating an inhibitor of a receptor tyrosine kinase ligand to a subject in need thereof.